

09593173

=> d his

(FILE 'HOME' ENTERED AT 11:41:46 ON 07 MAR 2005)

FILE 'REGISTRY' ENTERED AT 11:41:57 ON 07 MAR 2005

L1           STRUCTURE UPLOADED  
L2           0 S L1  
L3           0 S L1 SSS FULL  
L4           STRUCTURE UPLOADED  
L5           4 S L4  
L6           40 S L4 SSS FULL

FILE 'CAPLUS' ENTERED AT 11:46:51 ON 07 MAR 2005

L7           10 S L6

FILE 'REGISTRY' ENTERED AT 11:51:44 ON 07 MAR 2005

FILE 'MARPAT' ENTERED AT 11:51:51 ON 07 MAR 2005

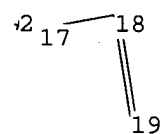
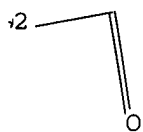
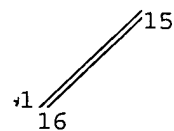
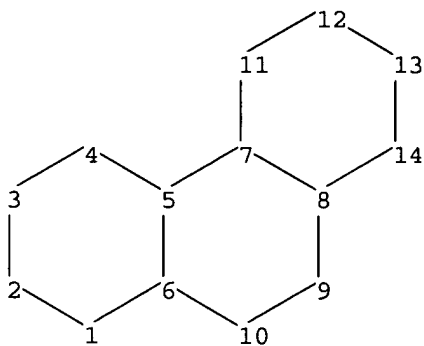
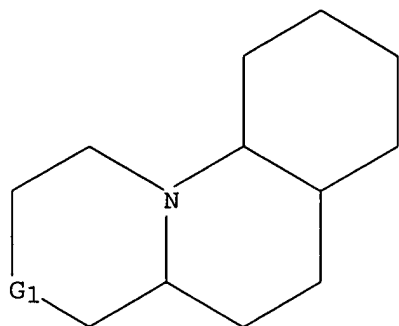
L8           0 S L6  
L9           8 S L6 SSS FULL  
L10          5 S L9/COMPLETE

FILE 'CAPLUS' ENTERED AT 11:53:49 ON 07 MAR 2005

L11          3 S L10 NOT L7  
             E GUARNA A/IN  
L12          6 S E4  
L13          4 S L12 NOT L7

=>

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chain nodes :

15 16 17 18 19

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds :

15-16 17-18 18-19

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12 12-13 13-14

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-14 9-10 15-16 17-18 18-19

exact bonds :

11-12 12-13 13-14

isolated ring systems :

containing 1 :

G1:NO2, [\*1], [\*2]

Match level :

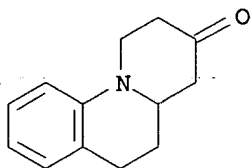
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1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS  
19:CLASS

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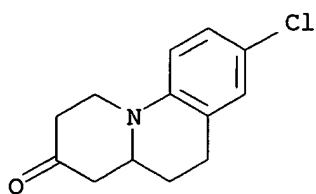
=> d 1-10 bib abs hitstr

L7 .ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:690879 CAPLUS  
DN 141:360203  
TI Benzo[c]quinolizin-3-ones Theoretical Investigation: SAR Analysis and Application to Nontested Compounds  
AU Braga, S. F.; Galvao, D. S.  
CS Instituto de Fisica Gleb Wataghin, Universidade Estadual de Campinas, Campinas, 13083-970, Brazil  
SO Journal of Chemical Information and Computer Sciences (2004), 44(6), 1987-1997  
CODEN: JCISD8; ISSN: 0095-2338  
PB American Chemical Society  
DT Journal  
LA English  
AB We investigate with the use of theor. methodologies the activity of a set of 47 benzo[c]quinolizin-3-ones (BC3), some of them explored as selective inhibitors of the human 5 $\alpha$ -reductase steroid. For the structure-activity study we have considered dividing the mols. into groups of tested and nontested compds. Semiempirical calcns. and pattern recognition methods such as Electronic Indexes Methodol. (EIM), Principal Components Anal. (PCA), Hierarchical Cluster Anal. (HCA), and K-Nearest Neighbors (KNN) have been applied to search for a correlation between exptl. activity and theor. descriptors. Our results show that it is possible to directly correlate some mol. quantum descriptors with BC3 biol. activity. This information can be used in principle to identify active/inactive untested compds. and/or to design new active compds.  
IT 194979-79-8 194979-82-3 194979-83-4  
307335-24-6 307335-25-7 307335-26-8  
307335-27-9 307335-28-0 307335-30-4  
307335-31-5 307335-32-6 307335-33-7  
758719-96-9 758719-97-0 758719-98-1  
758719-99-2 758720-00-2 758720-01-3  
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(benzo[c]quinolizin-3-ones theor. investigation for SAR anal. and application to nontested compds.)  
RN 194979-79-8 CAPLUS  
CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX NAME)



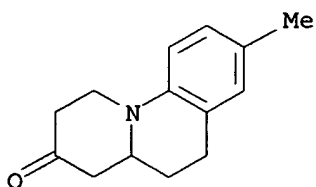
RN 194979-82-3 CAPLUS  
CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX NAME)

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RN 194979-83-4 CAPLUS

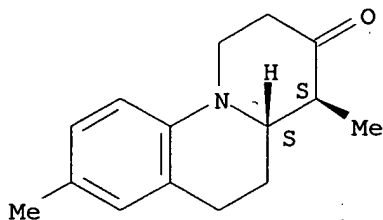
CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-8-methyl- (9CI) (CA INDEX NAME)



RN 307335-24-6 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4,8-dimethyl-, (4R,4aR)-rel- (9CI) (CA INDEX NAME)

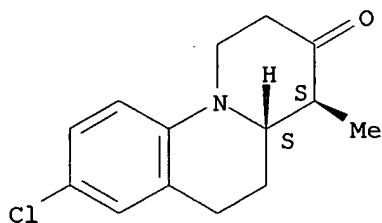
Relative stereochemistry.



RN 307335-25-7 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4-methyl-, (4R,4aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

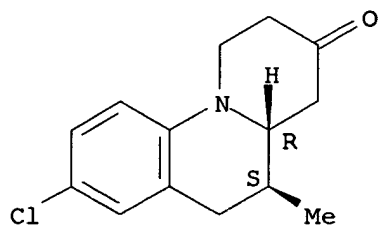


RN 307335-26-8 CAPLUS

09593173

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-5-methyl-,  
(4aR,5S)-rel- (9CI) (CA INDEX NAME)

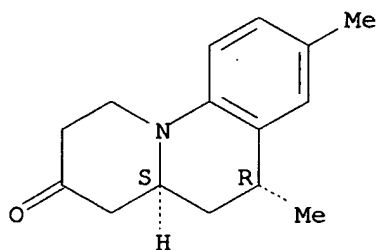
Relative stereochemistry.



RN 307335-27-9 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-6,8-dimethyl-,  
(4aR,6S)-rel- (9CI) (CA INDEX NAME)

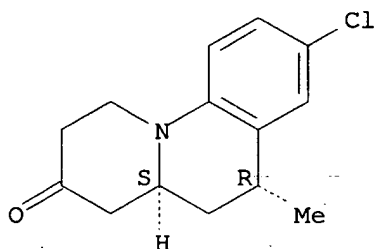
Relative stereochemistry.



RN 307335-28-0 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-6-methyl-,  
(4aR,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

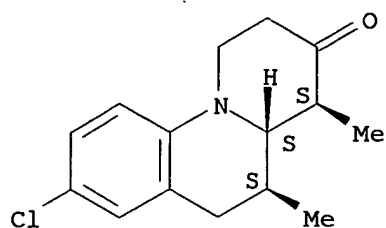


RN 307335-30-4 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4,5-dimethyl-,  
(4R,4aR,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

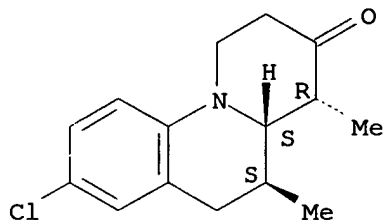
09593173



RN 307335-31-5 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4,5-dimethyl-, (4R,4aS,5S)-rel- (9CI) (CA INDEX NAME)

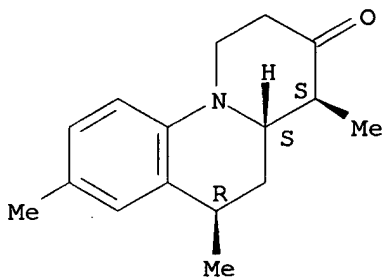
Relative stereochemistry.



RN 307335-32-6 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4,6,8-trimethyl-, (4R,4aR,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

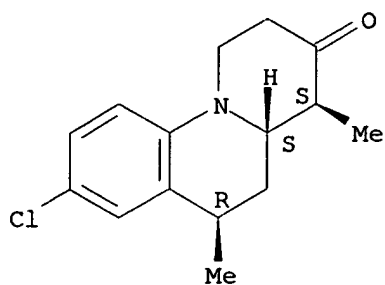


RN 307335-33-7 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4,6-dimethyl-, (4R,4aR,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

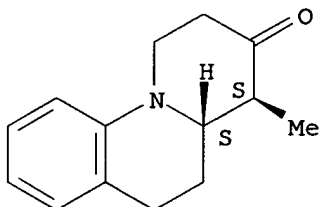
09593173



RN 758719-96-9 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4-methyl-,  
(4R,4aR)-rel- (9CI) (CA INDEX NAME)

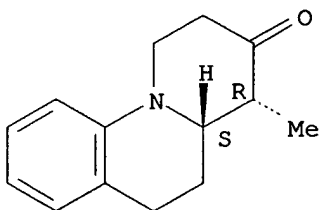
Relative stereochemistry.



RN 758719-97-0 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4-methyl-,  
(4R,4aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



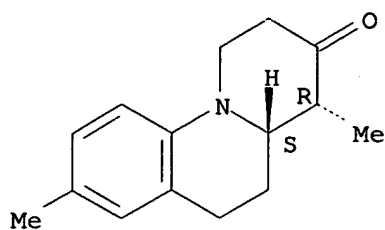
RN 758719-98-1 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4,8-dimethyl-,  
(4R,4aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



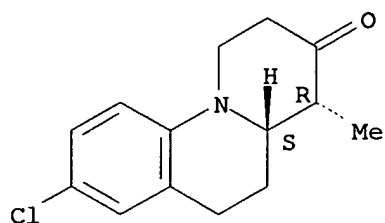
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RN 758719-99-2 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4-methyl-, (4R,4aS)-rel- (9CI) (CA INDEX NAME)

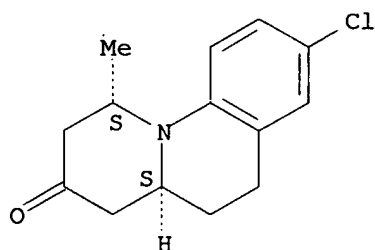
Relative stereochemistry.



RN 758720-00-2 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-1-methyl-, (1R,4aR)-rel- (9CI) (CA INDEX NAME)

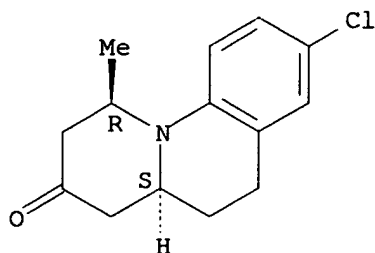
Relative stereochemistry.



RN 758720-01-3 CAPLUS

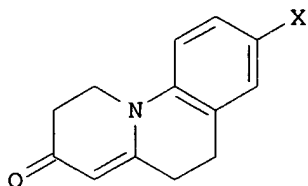
CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-1-methyl-, (1R,4aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2000:632698 CAPLUS  
DN 133:362693  
TI Benzo[c]quinolizin-3-ones: A Novel Class of Potent and Selective  
Nonsteroidal Inhibitors of Human Steroid 5 $\alpha$ -Reductase 1  
AU Guarna, Antonio; Machetti, Fabrizio; Occhiato, Ernesto G.; Scarpi, Dina;  
Comerci, Alessandra; Danza, Giovanna; Mancina, Rosa; Serio, Mario; Hardy,  
Kimber  
CS Dipartimento di Chimica Organica U. Schiff and Centro di Studio sulla  
Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni,  
Universita di Firenze, Florence, I-50121, Italy  
SO Journal of Medicinal Chemistry (2000), 43(20), 3718-3735  
CODEN: JMCMAR; ISSN: 0022-2623  
PB American Chemical Society  
DT Journal  
LA English  
GI



I

AB The synthesis and biol. evaluation of a series of novel, selective inhibitors of isoenzyme 1 of human 5 $\alpha$ -reductase (5 $\alpha$ R) (EC 1.3.99.5) are reported. The inhibitors are 4aH- or 1H-tetrahydrobenzo[c]quinolizin-3-ones bearing at positions 1, 4, 5, or 6 a Me group and at position 8 a hydrogen, Me group, or chlorine atom. All these compds. were tested toward 5 $\alpha$ R-1 and 5 $\alpha$ R-2 expressed in CHO cells (CHO 1827 and CHO 1829, resp.) resulting in selective inhibitors of the type 1 isoenzyme, with inhibitory potencies (IC<sub>50</sub>) ranging from 7.6 to 9100 nM. The inhibitors of the 4aH-series, having a double bond at position 1,2, were generally less active than the corresponding inhibitors of the 1H-series having the double bond at position 4,4a on the A ring. The presence of a Me group at position 4, associated with a substituent at position 8, determined the highest inhibition potency (IC<sub>50</sub> from 7.6 to 20 nM). The 1H-benzo[c]quinolizin-3-ones I [X = Me, Cl], having K<sub>i</sub> values of 5.8  $\pm$  1.8 and 2.7  $\pm$  0.6 nM, resp., toward 5 $\alpha$ R-1 expressed in CHO

cells, were also tested toward native 5 $\alpha$ R-1 in human scalp and 5 $\alpha$ R-2 in human prostate homogenates, in comparison with finasteride and the known 5 $\alpha$ R-1-selective inhibitor LY191704, and their mechanism of inhibition was determined. They both inhibited the enzyme through a reversible competitive mechanism and again were selective inhibitors of 5 $\alpha$ R-1 with IC50 values of 41 nM. These specific features make these inhibitors suitable candidates for further development as drugs in the treatment of DHT-dependent disorders such as acne and androgenic alopecia in men and hirsutism in women.

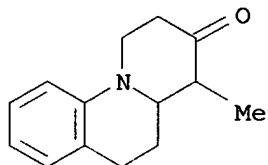
IT 5569-24-4P 194979-79-8P 194979-82-3P  
 194979-83-4P 307335-24-6P 307335-25-7P  
 307335-26-8P 307335-27-9P 307335-28-0P  
 307335-29-1P 307335-30-4P 307335-31-5P  
 307335-32-6P 307335-33-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of benzo[c]quinolizin-3-ones as potent and selective nonsteroidal inhibitors of human steroid 5 $\alpha$ -reductase 1)

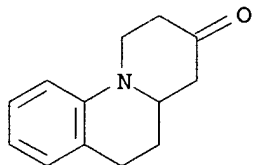
RN 5569-24-4 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



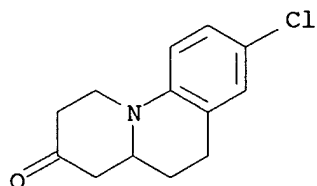
RN 194979-79-8 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX NAME)



RN 194979-82-3 CAPLUS

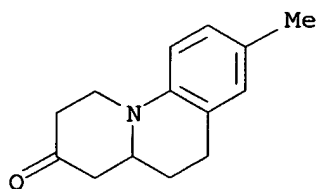
CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX NAME)



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RN 194979-83-4 CAPLUS

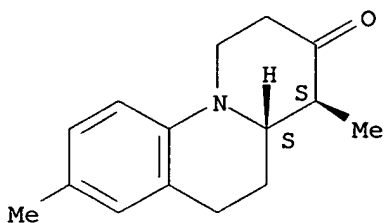
CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-8-methyl- (9CI) (CA INDEX NAME)



RN 307335-24-6 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4,8-dimethyl-, (4R,4aR)-rel- (9CI) (CA INDEX NAME)

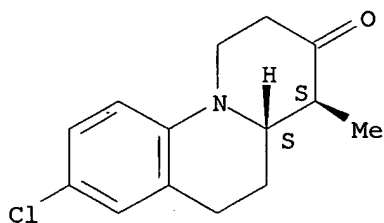
Relative stereochemistry.



RN 307335-25-7 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4-methyl-, (4R,4aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

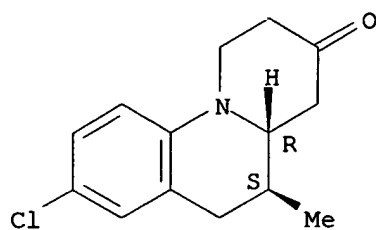


RN 307335-26-8 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-5-methyl-, (4aR,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

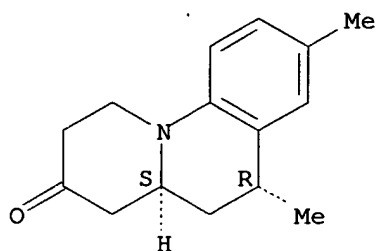
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RN 307335-27-9 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-6,8-dimethyl-,  
(4aR,6S)-rel- (9CI) (CA INDEX NAME)

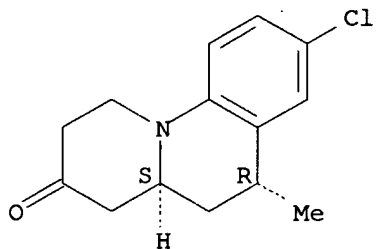
Relative stereochemistry.



RN 307335-28-0 CAPLUS

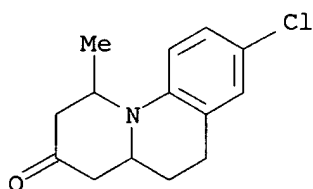
CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-6-methyl-,  
(4aR,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 307335-29-1 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-1-methyl-,  
(9CI) (CA INDEX NAME)

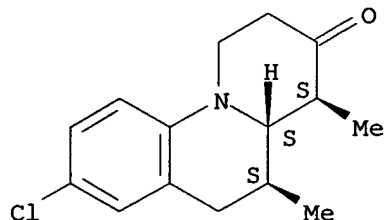


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RN 307335-30-4 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4,5-dimethyl-, (4R,4aR,5R)-rel- (9CI) (CA INDEX NAME)

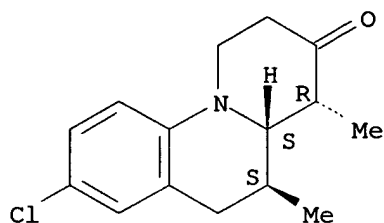
Relative stereochemistry.



RN 307335-31-5 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4,5-dimethyl-, (4R,4aS,5S)-rel- (9CI) (CA INDEX NAME)

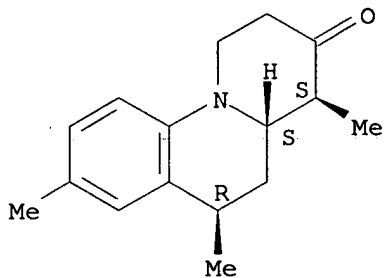
Relative stereochemistry.



RN 307335-32-6 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4,6,8-trimethyl-, (4R,4aR,6S)-rel- (9CI) (CA INDEX NAME)

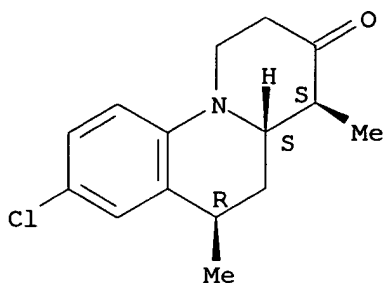
Relative stereochemistry.



RN 307335-33-7 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-4,6-dimethyl-, (4R,4aR,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:177171 CAPLUS

DN 132:317634

TI Synthesis of 8-chloro-benzo[c]quinolizin-3-ones as potent and selective inhibitors of human steroid 5 $\alpha$ -reductase 1

AU Guarna, Antonio; Occhiato, Ernesto G.; Scarpi, Dina; Zorn, Chiara; Danza, Giovanna; Commerci, Alessandra; Mancina, Rosa; Serio, Mario

CS Dipartimento di Chimica Organica "U. Schiff" and Centro di Studio sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, CNR, Universita di Firenze, Florence, I-50121, Italy

SO Bioorganic & Medicinal Chemistry Letters (2000), 10(4), 353-356  
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Science Ltd.

DT Journal

LA English

AB The synthesis of a series of differently substituted 8-chloro-benzo[c]quinolizin-3-ones, as potent and selective human steroid 5 $\alpha$ -reductase type 1 inhibitors, has been accomplished by a four-step procedure based on the TiCl<sub>4</sub>-promoted tandem Mannich-Michael cyclization of 2-silyloxy-1,3-butadienes with N-t-Boc iminium ions from quinolin-2-ones. The presence on the benzo[c]quinolizinone nucleus of a Me group and a double bond at positions 6 and 4-4a, resp., gave rise to one of the most potent non-steroidal steroid 5 $\alpha$ -reductase-1 inhibitors reported so far (IC<sub>50</sub> = 14 nM).

IT 267226-10-8P 267226-11-9P 267226-12-0P

267226-15-3P

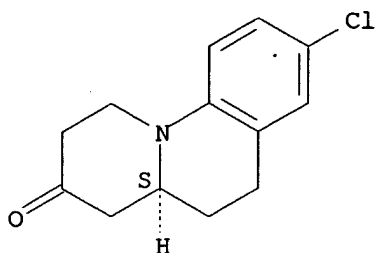
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis of chlorobenzoquinolizinones as potent and selective inhibitors of human steroid 5 $\alpha$ -reductase 1)

RN 267226-10-8 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-, (4aS)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

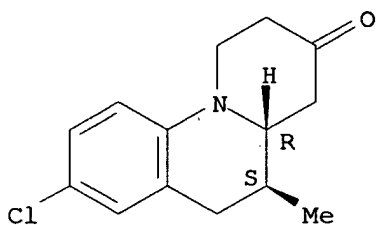
09593173



RN 267226-11-9 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-5-methyl-,  
(4aR,5S)- (9CI) (CA INDEX NAME)

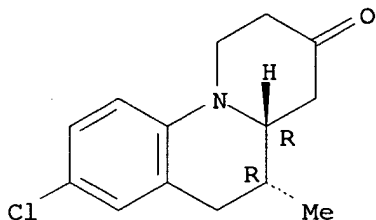
Absolute stereochemistry.



RN 267226-12-0 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-5-methyl-,  
(4aR,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

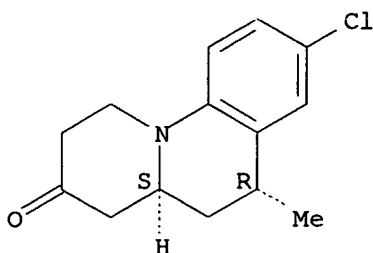


RN 267226-15-3 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-6-methyl-,  
(4aS,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





IT 267226-16-4P

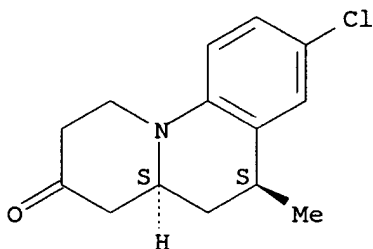
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis of chlorobenzoquinolizinones as potent and selective inhibitors of human steroid 5 $\alpha$ -reductase 1)

RN 267226-16-4 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro-6-methyl-, (4aS,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:113517 CAPLUS

DN 130:178758

TI Use of benzo[c]quinolizine derivatives as plant growth regulators

IN Guarna, Antonio; Serio, Mario

PA Applied Research Systems ARS Holding N.V., Neth. Antilles

SO PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905913	A1	19990211	WO 1998-EP4737	19980729
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				

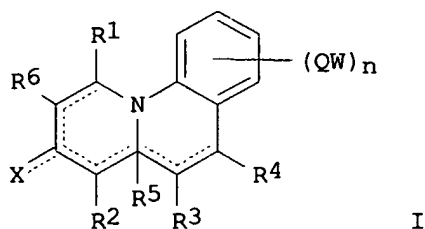
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2299465	AA	19990211	CA 1998-2299465	19980729
AU 9891570	A1	19990222	AU 1998-91570	19980729
AU 750092	B2	20020711		
EP 999747	A1	20000517	EP 1998-943798	19980729
EP 999747	B1	20030423		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2001511433	T2	20010814	JP 2000-504746	19980729
AT 237938	E	20030515	AT 1998-943798	19980729
PT 999747	T	20030829	PT 1998-943798	19980729
ES 2192332	T3	20031001	ES 1998-943798	19980729
US 6514912	B1	20030204	US 2000-480238	20000110

PRAI IT 1997-FI193 A 19970801  
 WO 1998-EP4737 W 19980729  
 OS MARPAT 130:178758  
 GI



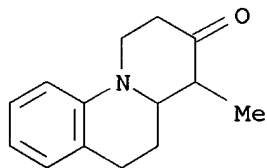
AB The benzo[c]quinolizine derivs. I (R1-4, R6 = H, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, etc.; R5 = H, alkyl, arylalkyl, CO<sub>2</sub>H, etc.; Q = bond, alkyl, alkenyl, alkynyl, CO, etc.; W = H, alkyl, alkenyl, aryl, etc.; n = 1-4; a, b, c, d, e, f and g are single or double bonds) are plant growth regulators.

IT 5569-24-4 194979-79-8 194979-82-3  
 194979-83-4 194979-84-5

RL: AGR (Agricultural use); BIOL (Biological study); USES (Uses)  
 (plant growth regulator)

RN 5569-24-4 CAPLUS

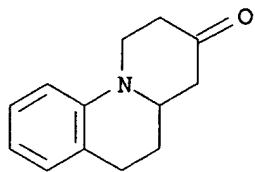
CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



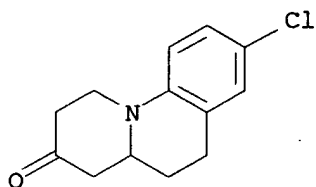
RN 194979-79-8 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX NAME)

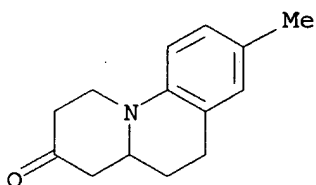
09593173



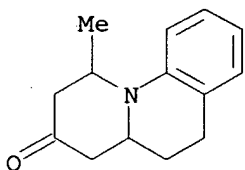
RN 194979-82-3 CAPLUS  
CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro- (9CI) (CA  
INDEX NAME)



RN 194979-83-4 CAPLUS  
CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-8-methyl- (9CI) (CA  
INDEX NAME)



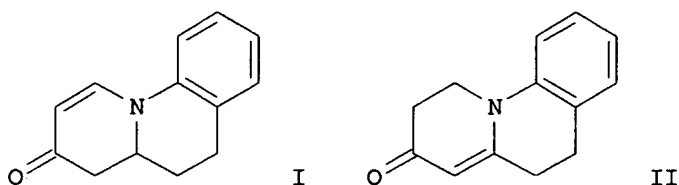
RN 194979-84-5 CAPLUS  
CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-1-methyl- (9CI) (CA  
INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1998:713257 CAPLUS  
DN 130:52313

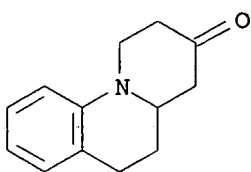
TI Synthesis of benzo[c]quinolizin-3-ones: selective non-steroidal inhibitors of steroid 5 $\alpha$ -reductase 1  
 AU Guarna, Antonio; Occhiato, Ernesto G.; Scarpi, Dina; Tsai, Ruey; Danza, Giovanna; Comerchi, Alessandra; Mancina, Rosa; Serio, Mario  
 CS Dipartimento di Chimica Organica "U. Schiff", Centro di Studio sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, CNR, Univ. di Firenze, Florence, I-50121, Italy  
 SO Bioorganic & Medicinal Chemistry Letters (1998), 8(20), 2871-2876  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 GI



AB A short and efficient synthesis of novel benzo[c]quinolizin-3-ones I and II is described. The synthesis is based on the tandem Mannich-Michael cyclization between 2-(silyloxy)-1,3-butadienes and a N-t-Boc iminium ion. I and II are selective inhibitors of human steroid 5 $\alpha$ -reductase isoenzyme 1, and thus have potential application as drugs for treatment of male pattern baldness and other DHT-dependent skin disorders.

IT **194979-79-8P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (benzo[c]quinolizin-3-ones as selective inhibitors of steroid 5 $\alpha$ -reductase 1)

RN 194979-79-8 CAPLUS  
 CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

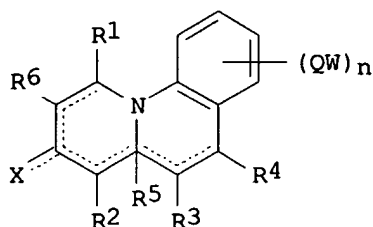
L7 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1997:542448 CAPLUS  
 DN 127:220585  
 TI Benzo[c]quinolizine derivatives, their preparation and use as 5 $\alpha$ -reductases inhibitors  
 IN Guarna, Antonio; Serio, Mario

PA Applied Research Systems ARS Holding N.V., Neth. Antilles; Guarna,  
Antonio; Serio, Mario  
SO PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9729107	A1	19970814	WO 1997-EP552	19970207
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2245758	AA	19970814	CA 1997-2245758	19970207
	AU 9717672	A1	19970828	AU 1997-17672	19970207
	AU 711886	B2	19991021		
	EP 880520	A1	19981202	EP 1997-903230	19970207
	EP 880520	B1	20030416		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EE 9800233	A	19981215	EE 1998-233	19970207
	EE 4058	B1	20030616		
	CN 1210536	A	19990310	CN 1997-192097	19970207
	CN 1116296	B	20030730		
	JP 2000504680	T2	20000418	JP 1997-528158	19970207
	SK 283299	B6	20030502	SK 1998-1044	19970207
	AT 237614	E	20030515	AT 1997-903230	19970207
	PT 880520	T	20030731	PT 1997-903230	19970207
	ES 2192263	T3	20031001	ES 1997-903230	19970207
	PL 187618	B1	20040831	PL 1997-328123	19970207
	EP 926148	A1	19990630	EP 1997-122733	19971223
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 9803444	A	19980724	NO 1998-3444	19980724
	US 6303622	B1	20011016	US 1998-117583	19980729
	CA 2315055	AA	19990708	CA 1998-2315055	19981221
	<del>WO 9933828</del>	<del>A1</del>	<del>19990708</del>	<del>WO 1998-EP8582</del>	<del>19981221</del>
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9924194	A1	19990719	AU 1999-24194	19981221
	AU 744105	B2	20020214		
	BR 9813836	A	20001010	BR 1998-13836	19981221
	EP 1066284	A1	20010110	EP 1998-966711	19981221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EE 200000387	A	20011217	EE 2000-200000387	19981221
	JP 2001527074	T2	20011225	JP 2000-526509	19981221
	ZA 9811762	A	19990623	ZA 1998-11762	19981222

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HK 1018783	A1	20031128	HK 1999-103821	19990903
NO 2000003199	A	20000823	NO 2000-3199	20000620
HK 1033128	A1	20040930	HK 2001-103695	20010529
US 2001044542	A1	20011122	US 2001-888952	20010625
US 6555549	B2	20030429		
US 2001047098	A1	20011129	US 2001-891088	20010625
US 6552034	B2	20030422		
PRAI IT 1996-FI19	A	19960209		
WO 1997-EP552	W	19970207		
EP 1997-122733	A	19971223		
US 1998-117583	A1	19980729		
WO 1998-EP8582	W	19981221		
OS MARPAT 127:220585				
GI				



I

AB The benzo[c]quinolizine derivs. I (R1-R4, R6 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycle, halo, amino azide, alkoxy carbonyl, etc.; R5 = H, alkyl, alkoxy carbonyl, cyano, aryl, heterocycle; X = O, acyl, alkoxy carbonyl, NO<sub>2</sub>, carbamoyl; Q = bond, alkyl, alkenyl, alkynyl, amino, etc., W = H, alkyl, alkenyl, alkynyl, aryl, aryloxy, amino, halo, etc.) were prepared as 5 $\alpha$ -reductases inhibitors (no data). Thus, N-(tert-butoxycarbonyl)-2-ethoxy-1,2,3,4-tetrahydroquinoline was cyclized with 2-(trimethylsilyloxy)-1,3-butadiene to give 1,2,4,4a,5,6-hexahydro-(11H)-benzo[c]quinolizin-3-one.

IT **5569-24-4P 194979-79-8P 194979-82-3P**

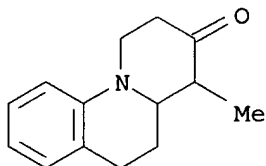
**194979-83-4P 194979-84-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of benzo[c]quinolizine derivs. as 5 $\alpha$ -reductases inhibitors)

RN 5569-24-4 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

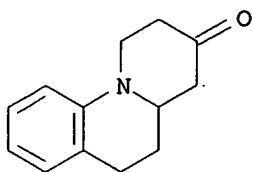


RN 194979-79-8 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX

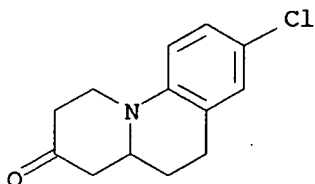
09593173

NAME)



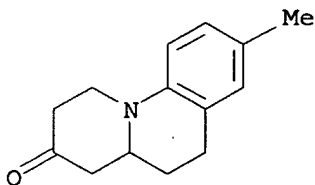
RN 194979-82-3 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 8-chloro-1,2,4,4a,5,6-hexahydro- (9CI) (CA INDEX NAME)



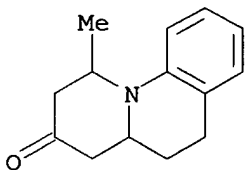
RN 194979-83-4 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-8-methyl- (9CI) (CA INDEX NAME)



RN 194979-84-5 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-1-methyl- (9CI) (CA INDEX NAME)



L7 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1966:84768 CAPLUS  
DN 64:84768

OREF 64:15941e-h,15942c

TI Preparation and chemistry of 10 $\alpha$ -estra-4-en-3-ones

AU Farkas, Eugene; Owen, John M.; Debono, M.; Molloy, R. M.; Marsh, Max M.

CS Eli Lilly &amp; Co., Indianapolis, IN

SO Tetrahedron Letters (1966), (10), 1023-7

CODEN: TELEAY; ISSN: 0040-4039

DT Journal

LA English

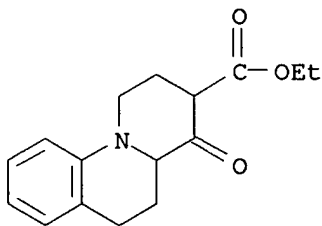
OS CASREACT 64:84768

AB cf. CA 54, 21197b. The substituted estra-4,8(10)-dien-3-ones (I, R = H, Me) in alc. hydrogenated with one equivalent H on Pd-BaSO<sub>4</sub> or Pd-Al<sub>2</sub>O<sub>3</sub> gave small amts. of the appropriately substituted 5 $\alpha$ ,10 $\alpha$ -estrane (II, R = H, Me) (III, IV) and 20-30% yield of the corresponding 4-en-3-ones (V, R = H, Me) (VI, VII). In general, higher yields (60-80%) of V were obtained by use of 2% Pd-SrCO<sub>3</sub> in C<sub>6</sub>H<sub>6</sub> though these alternative conditions were not applicable in some redns. owing to solubility differences. VI, m. 172-3°,  $\lambda$  245  $\mu$  ( $\epsilon$  15,800), showed an optical rotatory dispersion (O.R.D.) curve almost identical with that of the corrected curve for 10 $\alpha$ -testosterone. The  $\pi$ - $\pi^*$  portion of the curve indicating the chirality of the chromophore showed a neg. Cotton effect, best accommodated by assumption of half-chair and boat formations for the A and B rings and with cis diaxial 2 $\alpha$ ,10 $\alpha$  protons. The upfield shift of the 18-Me protons at 42 cycles/sec. (cps.) as compared to 50 cps. in the N.M.R. spectrum of 19-nortestosterone (VIII) confirmed the boat conformation of the B ring. VI was readily isomerized to VIII by HCl in CHCl<sub>3</sub> or with aqueous KOBu. Further confirmation of the structure of VI was obtained by the catalytic hydrogenation of the remaining double bond to give the known III. VI was acetylated in Ac<sub>2</sub>O-C<sub>5</sub>H<sub>5</sub>N to the acetate, m. 143-4°, and oxidation of VI in C<sub>5</sub>H<sub>5</sub>N gave high yields of 10 $\alpha$ -estra-4-ene-3,17-dione, m. 162-4°. Metal-ammonia reduction of VI yielded 20% 5 $\alpha$ ,10 $\alpha$ -estrane-3-on-17 $\beta$ -ol, together with a 60% yield of the 5 $\beta$ ,9 $\alpha$ ,10 $\alpha$ -estrane (IX), m. 121-2°. IX exhibited on O.R.D. curve with neg. Cotton effect  $[\phi] - 1022^\circ$  ( $\lambda$  314 m $\mu$ , in agreement with octant rule predictions. Hydrogenation of I (R = Me) gave VII, m. 193-5°,  $\lambda$  243  $\mu$  ( $\epsilon$  16,400) together with IV as a by-product. The O.R.D. and N.M.R. spectra of VII showed the salient features of I (R = H). VI showed no androgenic activity but maintained a high pituitary agonadotrophin inhibitory activity. A weak uterotrophic response was also noted.

IT 4527-67-7, 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-oxo-, ethyl ester, hydrochloride (preparation of)

RN 4527-67-7 CAPLUS

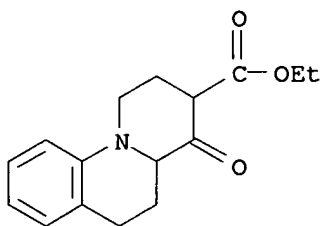
CN 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-oxo-, ethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl



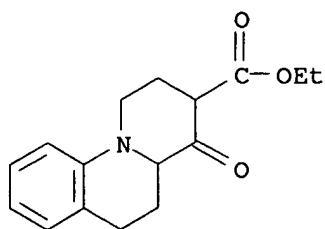
L7 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1966:84767 CAPLUS  
 DN 64:84767  
 OREF 64:15941e  
 TI Azasteroids. III. Approaches to 9-azasteroids  
 AU Schleigh, W. R.; Popp, F. D.  
 CS Clarkson Coll. of Technol., Potsdam, NY  
 SO Journal of the Chemical Society [Section] C: Organic (1966), (8), 760-2  
 CODEN: JSOOAX; ISSN: 0022-4952  
 DT Journal  
 LA English  
 OS CASREACT 64:84767  
 AB cf. CA 64, 5161d. Some unsuccessful approaches to 9-azasteroids are described. 3-Deoxy-18-nor-9,15,16-triaza-814(15)-estrone has been prepared  
 IT **4527-67-7**, 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-oxo-, ethyl ester, hydrochloride (preparation of)  
 RN 4527-67-7 CAPLUS  
 CN 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-oxo-, ethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L7 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1966:84766 CAPLUS  
 DN 64:84766  
 OREF 64:15941d-e  
 TI Viridin. V. Structure  
 AU Grove, J. F.; McCloskey, P.; Moffatt, J. S.  
 CS Imp. Chem. Ind. Ltd., Welwyn, UK  
 SO Journal of the Chemical Society [Section] C: Organic (1966), (8), 743-7  
 CODEN: JSOOAX; ISSN: 0022-4952  
 DT Journal  
 LA English  
 GI For diagram(s), see printed CA Issue.  
 AB cf. preceding abstract The structure of viridin (I), C<sub>20</sub>H<sub>16</sub>O<sub>6</sub>, an antifungal metabolic product of *Gliocladium virens*, is elucidated.  
 IT **4527-67-7**, 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-oxo-, ethyl ester, hydrochloride (preparation of)  
 RN 4527-67-7 CAPLUS  
 CN 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-oxo-,

ethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

L7 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1966:35773 CAPLUS

DN 64:35773

OREF 64:6613b-h, 6614a-h, 6615a-h, 6616a-b

TI Synthesis of 9-azasteroids. II. Synthesis of  $\beta$ -cyano- and  $\beta$ -carbethoxy-3-and 4-oxo-1,2,3,4,5,6-hexahydrobenzo[c]quinolizines

AU Jones, G.; Wood, J.

CS Univ. Keele, UK

SO Tetrahedron (1965), 21(10), 2961-71

CODEN: TETRAB; ISSN: 0040-4020

DT Journal

LA English

OS CASREACT 64:35773

GI For diagram(s), see printed CA Issue.

AB cf. CA 64, 2048c. The synthesis of 3- and 4-oxo-1,2,3,4,5,6-hexahydrobenzo[c]quinolizines with reactive ester or nitrile groups situated so as to allow addition of a 4th ring (ring D of the final 9-azasteroid) was reported. The previously prepared oxo ester (I, 12.4 g.) in 100 ml. dry PhMe treated portionwise with 1.3 g. NaH (50% paraffin mull) and the mixture refluxed 1 hr. with stirring, the cooled solution treated with 9.63 g. MeI in 25 ml. PhMe and the stirred solution slowly heated in 1 hr. to boiling, refluxed 2 hrs. and the cooled mixture diluted with 100 ml. dry Et<sub>2</sub>O, the filtered solution evaporated and the brown oil (5.5 g.) separated on

Al<sub>2</sub>O<sub>3</sub> gave the alkylation product (II), b<sub>0.0002</sub> 125-30°, and its stereoisomer, b<sub>0.0002</sub> 140-5°. Alternative routes to the non-enolizable oxo ester (III) were investigated. EtOCH<sub>2</sub>CH<sub>2</sub>OH (300 g.) and 350 g. PBr<sub>3</sub> mixed slowly below 80° and stirred 1 hr. poured into 500 ml. ice-H<sub>2</sub>O and the washed and dried bromide distilled at 50 mm. gave 285 g. EtOCH<sub>2</sub>CH<sub>2</sub>Br. K (40.4 g.) in 800 ml. dry Me<sub>3</sub>COH stirred 30 min. at 50° with 150 g. MeCH(CO<sub>2</sub>Et)<sub>2</sub> and the mixture refluxed 2 hrs. with stirring with 178 g. EtOCH<sub>2</sub>CH<sub>2</sub>Br, the solvent evaporated and the residue treated at 0° with 400 ml. ice-H<sub>2</sub>O and Et<sub>2</sub>O yielded 161 g. EtOCH<sub>2</sub>CH<sub>2</sub>CM<sub>2</sub>(CO<sub>2</sub>Et)<sub>2</sub> (IV), b<sub>10</sub> 130-2°. The ester (26 g.) in 200 ml. absolute alc. saturated with HBr and kept 16 hrs., refluxed 2 hrs. and evaporated

in vacuo, the residual mixture poured into 50 ml. ice-H<sub>2</sub>O and the aqueous layer basified with NaHCO<sub>3</sub>, extracted with Et<sub>2</sub>O and the dried extract distilled yielded

74% substantially pure BrCH<sub>2</sub>CH<sub>2</sub>CM<sub>2</sub>(CO<sub>2</sub>Et)<sub>2</sub> (V), b<sub>11</sub> 138-40°. IV (102 g.) in 600 ml. 33% HBr boiled 6 hrs. with periodic distillation of EtBr,

and removal of HBr in vacuo, HBr distilled in vacuo and the distillate neutralized, saturated with NaCl and extracted with Et<sub>2</sub>O, the extracted lactone and

the carboxylactone distillation residue combined, heated 1 hr. at 200° and distilled yielded 73% 2-methyl-4-butyrolactone (VI), b<sub>11</sub> 81°. VI (32 g.) in 80 ml. absolute alc. saturated with HBr at 0° and the mixture kept 24 hrs. at 20°, resatd. with HBr and kept 12 hrs. before pouring onto 120 g. ice, the ester layer and Et<sub>2</sub>O washings of the aqueous layer combined and the washed and dried solution distilled gave material, b<sub>1.0</sub> 45-50°, contaminated with 10% VI. Further washing with H<sub>2</sub>O and distillation gave pure BrCH<sub>2</sub>CH<sub>2</sub>CHMeCO<sub>2</sub>Et (VII), b<sub>1.0</sub> 47°. VII (49 g.), 24 g. Et 1,2,3,4-tetrahydroquinaldinate, 32.3 g. anhydrous K<sub>2</sub>CO<sub>3</sub>, and 1 g. KI heated 6 hrs. at 160-70° with vigorous stirring and the cooled mixture treated with cold H<sub>2</sub>O and CHCl<sub>3</sub>, the CHCl<sub>3</sub> layer dried and distilled at 10 mm. to give 12.1 g. VI and the pressure reduced gave 8.9 g. fraction, b<sub>0.18</sub> 104-40°. Further distillation at 0.0006 mm. yielded 61% material, b<sub>0.0006</sub> 140-60°, redistd. to give pure Et N-(3-ethoxycarbonylbutyl)-1,2,3,4-tetrahydroquinaldinate (VIII), b<sub>0.0006</sub> 154-6°. VIII (11.5 g.), 21.5 g. V, and 10.6 g. anhydrous K<sub>2</sub>CO<sub>3</sub> heated 7 hrs. at 160° with stirring and the product fractionally distilled gave mainly VIII, 2-ethoxycarbonyl-2-methyl-4-butyrolactone, and 8% required Et N-[3,3-bis(ethoxycarbonyl)butyl]-1,2,3,4-tetrahydroquinaldinate, b<sub>0.0006</sub> 150°. VIII (8.65 g.) in 60 ml. dry xylene added in 30 min. to KOBu-tert (from 1.09 g. K) in 50 ml. refluxing xylene with distillation of evolved BuOH, the cooled mixture diluted with 300 ml. dry Et<sub>2</sub>O and the hygroscopic K salt (6.0 g.) converted to the unstable base gave the acyloin (IX), HCl salt, m. 96-7°. Since the major difficulty in alkylating the cyclic ester I appeared to be competitive N-alkylation the basicity of the N was deactivated by nitration in the para-position using N<sub>2</sub>O<sub>4</sub> in CCl<sub>4</sub> according to Schaarschmidt et al. (CA 19, 2036). Et N-(3-ethoxycarbonylpropyl)-1,2,3,4-tetrahydroquinaldinate (X, R = H, 5.0 g.) in 50 ml. dry CCl<sub>4</sub> at -5° stirred vigorously with 1.6 g. powdered CaCO<sub>3</sub> with addition of 1.45 g. N<sub>2</sub>O<sub>4</sub> in 20 ml. CCl<sub>4</sub> and the mixture stirred 3 hrs. at -5°, warmed slowly and filtered at 20°, washed with 100 ml. cold 3N HCl, saturated aqueous NaHCO<sub>3</sub>, and H<sub>2</sub>O and the dried solution evaporated

yielded 83% brown oil. A sample distilled in a bulb tube gave X (R = NO<sub>2</sub>) (XI), b<sub>0.001</sub> 200-10°. I (4.77 g.) in 100 ml. CCl<sub>4</sub> at -5° stirred 30 min. with addition of 1.69 g. N<sub>2</sub>O<sub>4</sub> in 40 ml. ice-cold CCl<sub>4</sub> and the mixture stirred 3 hrs., the solution decanted at 20° and the decantation and CCl<sub>4</sub> washings evaporated yielded 24% solid. Recrystn. of a sample gave the nitro oxoester (XII, R = H) (XIII), m. 126-9°. XIII (1.35 g.) in 30 ml. PhMe added slowly to 50 ml. refluxing PhMe containing of KOBu-tert (from 0.18 K) and the mixture refluxed 30 min., the cooled mixture treated with 1.2 g. MeI in 20 ml. PhMe and the mixture slowly heated and refluxed 3 hrs., cooled and the filtered solution evaporated gave an unstable gum, corresponding to the expected methylated compound XII (R = Me). XI (0.66 g.) in 100 ml. alc. hydrogenated over 0.1 g. prereduced PtO<sub>2</sub> with adsorption of 3 molar equivs. H gave 0.61 g. brown oil, distilled to give the amino diester X (R = NH<sub>2</sub>), b<sub>0.0003</sub> 185-95°. The previously synthesized cyano ester (XIV, 8.16 g.) in 75 ml. xylene added in 1 hr. with stirring to 2.25 g. NaOEt in 75 ml. boiling xylene with slow distillation, the stirred mixture refluxed 1 hr. and distilled to vapor temperature 138°, the ice-cold suspension diluted with 100 ml. each of Et<sub>2</sub>O and H<sub>2</sub>O and the organic layer extracted with 100 ml. N aqueous NaOH, the combined aqueous layers adjusted

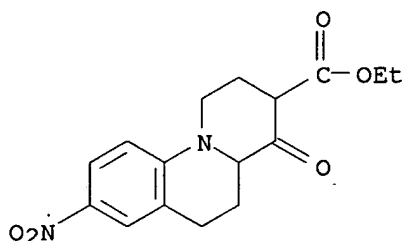
with 5N HCl at 0° to pH 6 and extracted with CHCl<sub>3</sub>, the residue on evaporation (6.41 g. brown gum) purified by regeneration from the HCl salt and a sample distilled gave 3-cyano-4-oxo-1,2,3,4,5,6-hexahydrobenzo[c]quinolizine, b<sub>0.003</sub> 180°; HCl salt, m. 163°

(decomposition). Nitration of the cyano ketone gave an extremely insol. brown solid which has not been characterized. The major difficulty in synthesis of 4-oxo-1,2,3,4,5,6-hexahydrobenzo[c]quinolizine derivs. appeared to be inherent instability of systems which are formally analogous to 3-oxo-N-phenylpiperidine and synthesis of the probably more stable 3-oxo derivs. was undertaken. Attempts to synthesize the potentially useful intermediate tricyclic oxo ester (XV, R = H) (XVI) were undertaken. The initial approach was that of cyclization of the diester, Et 1-(2-ethoxycarbonyl-ethyl)-1,2,3,4-tetrahydro-2-quinolyl acetate (XVII). Absolute alc. (300 ml.) and 4 ml. H<sub>2</sub>O containing 29.4 g. 2-quinolylacetoneitrile (from 2-chloromethylquinoline HCl salt) saturated with HCl at 60° and boiled 3 hrs., the chilled mixture filtered and the residue on evaporation in vacuo treated with ice-cold saturated aqueous NaHCO<sub>3</sub>, extracted with Et<sub>2</sub>O and the product distilled yielded 76% Et 2-quinolylacetate, b<sub>0.5</sub> 136-7°. The acetate (36.65 g.) in 250 ml. AcOH hydrogenated over prerduced PtO<sub>2</sub> with 2 moles H and the residue on evaporation treated with aqueous NaHCO<sub>3</sub> and Et<sub>2</sub>O, the Et<sub>2</sub>O layer dried and distilled yielded 92% Et 1,2,3,4-tetrahydro-2-quinolylacetate (XVIII), b<sub>0.6</sub> 130-8°; 1-benzoyl derivative, m. 96.5-7.0° (ligroine). XVIII (10 g.), 16.42 g. BrCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et (b<sub>2.5</sub> 44°), 9.5 g. finely ground K<sub>2</sub>CO<sub>3</sub>, and 0.38 g. KI heated 4 hrs. at 140° under a short air condenser and the cooled mixture treated with H<sub>2</sub>O and Et<sub>2</sub>O, the Et<sub>2</sub>O layer and washings dried and evaporated, the residual oil distilled at 12 mm. to give 4 g. BrCH<sub>2</sub>-CH<sub>2</sub>CO<sub>2</sub>Et and at 0.003 mm. gave 1.7 g. XVIII and 63% yield of XVII, b<sub>0.003</sub> 145-60°, redistd. to give a sample, b<sub>0.003</sub> 161°. XVII (12.0 g.) cyclized with EtONa (from 0.95 g. Na in 200 ml. xylene) and the chilled (0°) mixture treated with 100 ml. H<sub>2</sub>O, the aqueous layer adjusted to pH 6.5 and diluted with Et<sub>2</sub>O, the organic layer and subsequent Et<sub>2</sub>O exts. combined and evaporated gave 93% viscous orange oil, purified by regeneration from the HCl salt to give the alternative quinazoline (XIX, R = H) (XX); HCl salt, m. 130° (Me<sub>2</sub>CO-Et<sub>2</sub>O-HCl). The cyclized Na salt suspension from 6.0 g. XVII treated at 0° with 3.06 g. MeI in 25 ml. xylene, stirred 1 hr. at 20 and 8 hrs. at 60°, the cooled mixture filtered and the filtrate and Et<sub>2</sub>O washings evaporated, the light-brown oily mixture (3.86 g.) chromatographed on neutral Al<sub>2</sub>O<sub>3</sub> from ligroine-C<sub>6</sub>H<sub>6</sub> gave XV (R = Me) (XXI), b<sub>0.0004</sub> 130-4°, and the major isomer (XIX, R = Me) (XXII), b<sub>4</sub> 150-5°. The light brown oil (2 g., prepared as above) boiled 6 hrs. in 5N HCl and evaporated, the residue treated with aqueous NaHCO<sub>3</sub> and the free base extracted with Et<sub>2</sub>O yielded 73% 2-methyl-3-oxo-1,2,3,4,-5,6-hexahydrobenzo[c]quinolizine (XXIII), b<sub>0.003</sub> 130-40°. After equilibration with alc. EtONa the redistd. XXIII showed only the doublet at 0.99 ppm. Further confirmation that XXIII was a mixture of epimers and not of structural isomers was obtained by hydrolyzing and decarboxylating 0.223 g. of the pure major isomer XXII to give 88% XXIII, practically identical with that obtained from the mixture of oxo esters XXII. The equilibrated ketone XXIII heated 15 min. at 100° with a molar equivalent of 2,4-(O<sub>2</sub>N)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>NHNH<sub>2</sub> in absolute alc./HBr and the cooled mixture filtered, the salt taken up in CHCl<sub>3</sub> and shaken vigorously with aqueous Na<sub>2</sub>CO<sub>3</sub> and H<sub>2</sub>O, dried and evaporated gave XXIII dinitrophenylhydrazone, m. 195-8°. To identify the ketone and hence to deduce the direction of the Dieckmann cyclization in the di-ester XVII, attempts were made to synthesize XXIII or its isomer 4-methyl-3-oxo-1,2,3,4,5,6-hexahydrobenzo[c]quinolizine (XXIV), but attempts to alkylate XVIII with Me<sub>2</sub>CBrCO<sub>2</sub>Et were unsuccessful in the production of XXIII. Quinaldylolithium (from 252 g. quinaldine) in Et<sub>2</sub>O added to 268 g. MeI under gentle reflux and the mixture refluxed 1 hr., kept 16 hrs. at 20° and treated with 1300 ml. 5N HCl, the acid layer separated and the

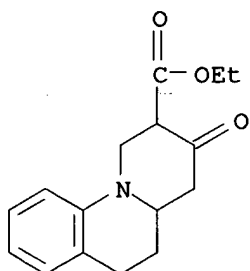
Et<sub>2</sub>O layer extracted with acid, the combined acid layers basified with NH<sub>4</sub>OH (d. 0.880) and the bases extracted with Et<sub>2</sub>O gave 47 g. quinaldine and 57% yield of 2-ethylquinoline, b<sub>14</sub> 134-5°. A filtered solution of PhLi (from 90 g. PhBr) added slowly with stirring to 75 g. 2-ethylquinoline in 100 ml. Et<sub>2</sub>O and the mixture refluxed 1 hr., the filtered 2-ethylquinolyl lithium added in 1 hr. with stirring to 34 g. Et<sub>2</sub>CO<sub>3</sub> in 100 ml. Et<sub>2</sub>O and the mixture boiled 3 hrs., the cooled solution treated with 500 ml. ice-cold 5N HCl, the acid layer and acid exts. neutralized with NH<sub>4</sub>OH and extracted with Et<sub>2</sub>O, evaporated and the residue distilled gave 29 g. 2-ethylquinoline b<sub>0.05</sub> 60-85°, and 15% yield of Et 2-(2-quinolyl)propionate (XXV), b<sub>0.05</sub> 116°; picrate, m. 137-40° (alc.). XXV (15.8 g.) in 150 ml. AcOH hydrogenated over 0.3 g. prerduced PtO<sub>2</sub> with 2 moles H, the filtered solution evaporated and the residue shaken with aqueous NaHCO<sub>3</sub> and Et<sub>2</sub>O, the Et<sub>2</sub>O extract dried and distilled gave 85% tetrahydro ester (XXVI) (R = H, R' = CHMeCO<sub>2</sub>Et) (XXVII), b<sub>0.7</sub> 134-8°. XXVII (13.9 g.), 21.5 g. BrCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et, 12.4 g. K<sub>2</sub>CO<sub>3</sub>, and 0.5 g. KI vigorously stirred 6 hrs. at 150° and the cooled product worked up as for XVII gave mainly 8.18 g. XXVII, b<sub>0.002</sub> 90-120°, and a 73% yield of the diester XXVI (R = CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et, R' = CHMeCO<sub>2</sub>Et) (XXVIII), b<sub>0.002</sub> 148-54°. XXVIII (6.48 g.) in 50 ml. xylene added slowly to KO<sub>2</sub>Me<sub>3</sub> (from 0.836 g. K) in 75 ml. boiling xylene with slow distillation continued 1 hr., the cooled mixture treated with 100 ml. ice-H<sub>2</sub>O and acidified to pH 6, extracted with Et<sub>2</sub>O and the residue on evaporation gave 2-ethoxycarbonyl-4-methyl-3-oxo-1,2,3,4,5,6-hexahydrobenzo[c]quinolizine (XXIX); HCl salt, melting to a thick glass at 50-5°, mobile at 85-90°. XXIX (2.5 g.) boiled 5 hrs. in 50 ml. 5N HCl and the residue on evaporation at 14 mm. treated with saturated aqueous NaHCO<sub>3</sub> and Et<sub>2</sub>O, the Et<sub>2</sub>O extract dried and distilled gave a ketone, recrystn. from ligroine gave colorless rods, m. 96-7°; 2,4-dinitrophenylhydrazone, m. 153-5°. XXIII and XXIV differed markedly in ir absorption between 1450 and 700 cm.<sup>-1</sup> and had retention times of 16.0 and 14.8 min. at 150°. Accordingly the C-methylation decarboxylation product was XXIII, the methylated keto ester XXII and the Dieckmann cyclization of XVII gave the oxo ester XX, unsuitable for further use in a 9-azasteroid synthesis. In view of the high yield obtained in cyclization of the cyano ester XIV it was decided finally to prepare and cyclize the isomeric cyano ester XXVI (R = CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et, R' = CH<sub>2</sub>CN) (XXX). XVIII (18 g.) in 500 ml. dry MeOH saturated with NH<sub>3</sub> at 0° and autoclaved 40 hrs. at 100°, the solution evaporated and the gum triturated with ligroine yielded 85% XXVI (R = H R' = CH<sub>2</sub>CONH<sub>2</sub>) (XXXI), m. 98-103°, recrystd. from C<sub>5</sub>H<sub>6</sub> to give a sample m. 103-4°; N-Bz derivative, m. 198-201° (alc.). XXXI (12.5 g.) and 5.93 g. NaCl in 60 ml. ClCH<sub>2</sub>CH<sub>2</sub>Cl stirred 15 min. with addition of 8.93 g. POCl<sub>3</sub> in 10 ml. ClCH<sub>2</sub>CH<sub>2</sub>Cl, the mixture warmed and boiled with stirring 12 hrs., the cooled mixture treated with 8.0 g. NaOH in MeOH and shaken out twice with cold brine, the organic layer dried and distilled yielded 72% XXVI (R = H, R' = CH<sub>2</sub>CN) (XXXII), b<sub>0.06</sub> 124-7°; N-Bz derivative, m. 130° (alc.). XXXII (5.0 g.), 10.47 g. BrCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et, 6.02 g. K<sub>2</sub>CO<sub>3</sub>, and 0.24 g. KI heated 6 hrs. at 140° with stirring, the crude product isolated as for XVII and heated 8 hrs. at 145° with 10.5 g. BrCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et and 6 g. K<sub>2</sub>CO<sub>3</sub>, worked up again as for XVII to give 1.6 g. XXXII, b<sub>0.0006</sub> 110-35° and 80% yield of XXX, b<sub>0.0006</sub> 156-62°, m. 66° (ligroine). XXX (2.96 g.) in 50 ml. xylene added in 1 hr. with stirring to EtONa (from 0.275 g. Na) in 60 ml. boiling xylene and the boiling mixture stirred 1 hr., worked up as for the cyano ketone from XIV to give 82% light yellow solid, m. 132-8°, recrystd. from alc. to colorless rhombs of the cyano ketone (XXXIII), m. 135.0-7.5°; HCl salt, m. 133-41°

(Me<sub>2</sub>CO); phenylhydrazone, m. 166-7° (alc.). Since the yields are good throughout the synthesis the intermediate required for elaboration of ring D is available in quantity.

- IT **5100-53-8**, 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-8-nitro-4-oxo-, ethyl ester **5100-62-9**, 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-3-oxo-, ethyl ester, hydrochloride **5100-63-0**, 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-2-methyl-3-oxo-, ethyl ester **5100-64-1**, 3H-Benzo[c]quinolizine-3-one, 1,2,4,4a,5,6-hexahydro-2-methyl- **5100-70-9**, 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-methyl-3-oxo-, ethyl ester **5100-71-0**, 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-methyl-3-oxo-, ethyl ester, hydrochloride **5100-76-5**, 1H-Benzo[c]quinolizine-4-carbonitrile, 2,3,4,4a,5,6-hexahydro-3-oxo-, hydrochloride **5100-77-6**, 1H-Benzo[c]quinolizine-4-carbonitrile, 2,3,4,4a,5,6-hexahydro-3-oxo- **5161-92-2**, 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-3-oxo-, ethyl ester **5161-93-3**, 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-3,4a-dimethyl-4-oxo-, ethyl ester **5569-24-4**, 3H-Benzo[c]quinolizine-3-one, 1,2,4,4a,5,6-hexahydro-4-methyl- (preparation of)
- RN **5100-53-8** CAPLUS
- CN 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-8-nitro-4-oxo-, ethyl ester (7CI, 8CI) (CA INDEX NAME)



- RN **5100-62-9** CAPLUS
- CN 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-3-oxo-, ethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)

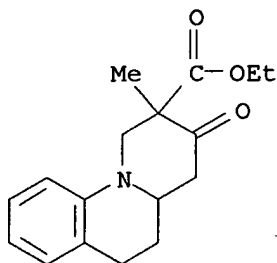


● HCl

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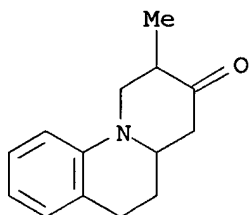
RN 5100-63-0 CAPLUS

CN 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-2-methyl-3-oxo-, ethyl ester (7CI, 8CI) (CA INDEX NAME)



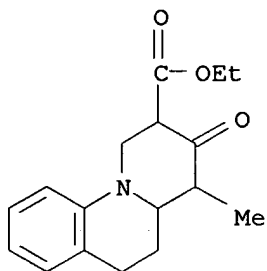
RN 5100-64-1 CAPLUS

CN 3H-Benzo[c]quinolizine-3-one, 1,2,4,4a,5,6-hexahydro-2-methyl- (7CI, 8CI) (CA INDEX NAME)



RN 5100-70-9 CAPLUS

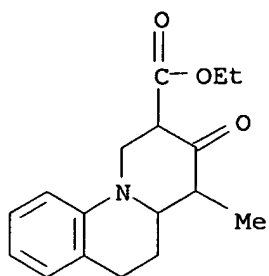
CN 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-methyl-3-oxo-, ethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 5100-71-0 CAPLUS

CN 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-4-methyl-3-oxo-, ethyl ester, hydrochloride (7CI, 8CI) (CA INDEX NAME)

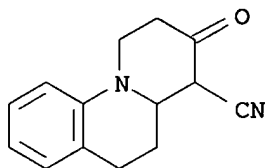
09593173



● HCl

RN 5100-76-5 CAPLUS

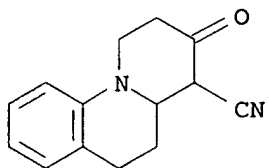
CN 1H-Benzo[c]quinolizine-4-carbonitrile, 2,3,4,4a,5,6-hexahydro-3-oxo-, hydrochloride (7CI, 8CI) (CA INDEX NAME)



● HCl

RN 5100-77-6 CAPLUS

CN 1H-Benzo[c]quinolizine-4-carbonitrile, 2,3,4,4a,5,6-hexahydro-3-oxo- (7CI, 9CI) (CA INDEX NAME)

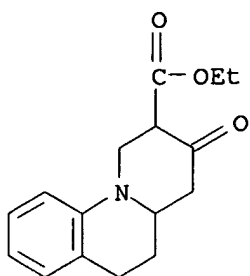


RN 5161-92-2 CAPLUS

CN 1H-Benzo[c]quinolizine-2-carboxylic acid, 2,3,4,4a,5,6-hexahydro-3-oxo-, ethyl ester (7CI, 8CI) (CA INDEX NAME)

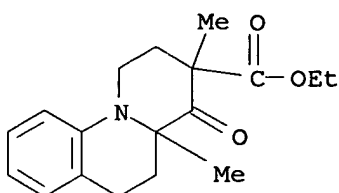


09593173



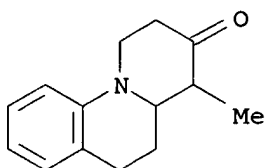
RN 5161-93-3 CAPLUS

CN 1H-Benzo[c]quinolizine-3-carboxylic acid, 2,3,4,4a,5,6-hexahydro-3,4a-dimethyl-4-oxo-, ethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 5569-24-4 CAPLUS

CN 3H-Benzo[c]quinolizin-3-one, 1,2,4,4a,5,6-hexahydro-4-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)



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=> d 1-3 bib abs

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:971589 CAPLUS

DN 140:13093

TI Use of benzo[c]quinolizinium derivatives for the treatment of diseases related to smooth muscle cell constriction

IN Becq, Frederic; Robert, Renaud; Pignoux Bulteau, Laurence; Rogier, Christian; Mettey Renoult, Yvette; Vierfond, Jean Michel; Joffre, Michel; Marivingt, Mounir Cecile

PA Centre National de la Recherche Scientifique CNRS, Fr.

SO Fr. Demande, 59 pp.

CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2840610	A1	20031212	FR 2002-6916	20020605
	WO 2003104228	A1	20031218	WO 2003-FR1688	20030605
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1509520	A1	20050302	EP 2003-757110	20030605
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	FR 2002-6916	A	20020605		
	WO 2003-FR1688	W	20030605		

OS MARPAT 140:13093

AB The invention discloses the use of benzo[c]quinolizinium derivs. (preparation included) for the treatment of diseases related to smooth muscle cell constriction, e.g. arterial hypertension and asthma.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:112345 CAPLUS

DN 128:167362

TI Preparation of benzo[c]quinolizinium salts and analogs as CFTR channel activators

IN Becq, Frederic; Mettey, Yvette; Vierfond, Jean-Michel; Verrier, Bernard; Gola, Maurice

PA Centre National de la Recherche Scientifique, Fr.; Becq, Frederic; Mettey, Yvette; Vierfond, Jean-Michel; Verrier, Bernard; Gola, Maurice

SO PCT Int. Appl., 128 pp.

CODEN: PIXXD2

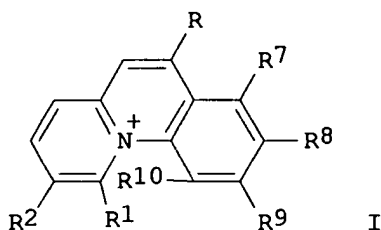
DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805642	A1	19980212	WO 1997-FR1436	19970731
	W:				
	CA, JP, US				

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
 FR 2751969 A1 19980206 FR 1996-9721 19960801  
 FR 2751969 B1 19981204  
 CA 2258924 AA 19980212 CA 1997-2258924 19970731  
 EP 937044 A1 19990825 EP 1997-936724 19970731  
 EP 937044 B1 20020130  
 R: CH, DE, FR, GB, IT, LI  
 JP 2000515863 T2 20001128 JP 1998-507677 19970731  
 US 6630482 B1 20031007 US 1999-230747 19990302  
 PRAI FR 1996-9721 A 19960801  
 WO 1997-FR1436 W 19970731  
 OS MARPAT 128:167362  
 GI



AB Title compds. (e.g., I.X; R1,R2 = H; R1R2 = atoms to complete a 6-membered aromatic ring; R7-R10 = H; 1 of R7-R10 may = halo; X = halide ion, ClO4-, etc.) were prepared Thus, 2-ClC6H4CN was cyclocondensed with 2-methylpyridine to give I.Cl-. Data for biol. activity of title compds. were given.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:315340 CAPLUS

DN 124:356152

TI Method for making negative lith images or direct-positive images

IN Dewanckele, Jean-Marie; Terrell, David; Andriessen, Hieronymus; Viaene, Kris

PA Agfa-Gevaert Naamloze Vennootschap, Belg.

SO Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 704751	A1	19960403	EP 1995-202566	19950922
	R: BE, DE, FR, GB, NL				
	JP 08220706	A2	19960830	JP 1995-271980	19950925
PRAI	EP 1994-202772	A	19940927		

OS MARPAT 124:356152

AB A method is provided for making neg. lithog. images or direct-pos. images by the steps of imagewise exposing a photog. light-sensitive silver halide material comprising a support, at least one internal latent image-type silver halide emulsion layer (in the case of direct-pos. materials) or surface latent image-type silver halide emulsion layer (in the case of lithog. materials) and development-nucleating amts. of a compound or a

precursor thereof, said compound having at least one quaternary heterocyclic ring system comprising at least three rings including a dihydropyridinium ring wherein carbon-nitrogen and carbon-carbon double bonds are also part of an aromatic ring, being one of said three rings, and wherein said double bonds and nitrogen atom in said dihydropyridinium ring are incorporated into annelated conjugated ring systems and developing said exposed photog. material in an alkaline surface developer, wherein said precursor is rapidly converted into a ring system as defined hereinbefore.

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L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2004:2706 CAPLUS  
 DN 140:53449  
 TI Pharmaceutical compositions for the treatment of diseases related to neurotrophins  
 IN **Guarna, Antonio**; Cozzolino, Federico; Torcia, Maria; Garaci, Enrico  
 PA Italy  
 SO PCT Int. Appl., 76 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004000324	A1	20031231	WO 2003-EP6471	20030618
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	IT 2002-FI107	A	20020619		

OS MARPAT 140:53449

AB The invention refers to pharmaceutical prepn. including as active compds. 3-aza-bicyclo[3.2.1]octane derivs. and/or their dimers acting as agonists of human neurotrophins. Therefore, such compds. are useful for treatment of diseases in which the neurotrophin functions are involved in defect, particularly of Nerve Growth Factor (NGF), such as neurodegenerative diseases of central nervous system (CNS), acquired immunodeficiency due to a reduced NGF bioavailability, or morbus conditions in which the stimulus of neoangiogenesis process is convenient.

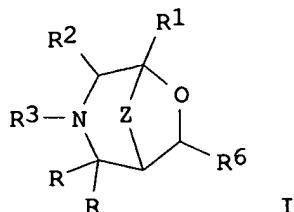
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:654699 CAPLUS  
 DN 135:211044  
 TI Preparation of 3-aza-6,8-dioxabicyclo[3.2.1]octanecarboxylates and analogs  
 IN **Guarna, Antonio**; Menchi, Gloria; Occhiato, Ernesto Giovanni; Machetti, Fabrizio; Scarpi, Dina  
 PA Universita Degli Studi di Firenze, Italy  
 SO Eur. Pat. Appl., 26 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1130022	A1	20010905	EP 2000-104135	20000229
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2401693	AA	20010907	CA 2001-2401693	20010227
	WO 2001064686	A1	20010907	WO 2001-EP2185	20010227
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,				

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HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, BF, BJ, CF, CG,  
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 US 2003176414 A1 20030918 US 2002-220556 20021101  
 PRAI EP 2000-104135 A 20000229  
 WO 2001-EP2185 W 20010227  
 OS CASREACT 135:211044; MARPAT 135:211044  
 GI



AB Title compds. [e.g., I; RR = O or each R = H; R1 = (un)substituted Ph; R2 = H, Me, CH2Ph; R3 = (un)substituted phenyl(methyl), CH(CO2H)CH2Ph, allyl, etc.; R6 = H, Me, CO2H, CH2OH; Z = O or NH] were prepared Thus, PhCOCH2NHCH2Ph was N-acylated by 1,4-dioxane-2,3-dicarboxylic acid monomethyl ester and the product cyclized to give I (RR = O, R1 = R3 = CH2Ph, R2 = H, R6 = CO2Me, Z = O). The method is suitable for solid phase synthesis and the preparation of combinatorial libraries.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:117047 CAPLUS

DN 132:151692

TI Preparation of (1H)-benzo[c]quinolizin-3-ones for use as 5α-reductase inhibitors

IN **Guarna, Antonio**; Serio, Mario; Occhiato, Ernesto Giovanni

PA Applied Research Systems Ars Holding N.V., Neth. Antilles

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

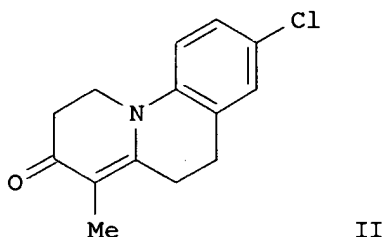
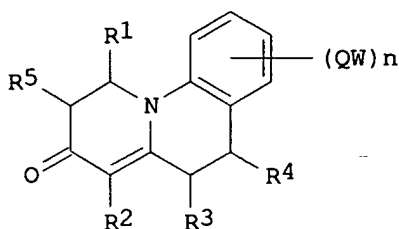
DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000008019	A1	20000217	WO 1999-EP5277	19990723
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338498	AA	20000217	CA 1999-2338498	19990723

AU 9963123	A1	20000228	AU 1999-63123	19990723
AU 751873	B2	20020829		
EP 1102765	A1	20010530	EP 1999-941269	19990723
EP 1102765	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100286	T2	20010723	TR 2001-200100286	19990723
BR 9912870	A	20011016	BR 1999-12870	19990723
EE 200100060	A	20020617	EE 2001-60	19990723
JP 2002522435	T2	20020723	JP 2000-563652	19990723
NZ 509243	A	20021126	NZ 1999-509243	19990723
CZ 291648	B6	20030416	CZ 2001-434	19990723
AT 250057	E	20031015	AT 1999-941269	19990723
CN 1128148	B	20031119	CN 1999-809204	19990723
PT 1102765	T	20031231	PT 1999-941269	19990723
ES 2203169	T3	20040401	ES 1999-941269	19990723
ZA 2001000365	A	20010726	ZA 2001-365	20010112
BG 105198	A	20011231	BG 2001-105198	20010130
NO 2001000559	A	20010201	NO 2001-559	20010201
US 6723850	B1	20040420	US 2001-743373	20010525
HK 1037368	A1	20040618	HK 2001-108153	20011120
PRAI EP 1998-114524	A	19980803		
WO 1999-EP5277	W	19990723		
OS MARPAT 132:151692				
GI				



AB Benzo[c]quinolizin-3-ones I [R, R1, R2, R3, R4, R5 = H, CN, N3, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, halogen, amino, alkyloxy, aryloxy, carboxy, carboxamido; Q = bond, CO, alkyl, alkenyl, alkynyl, cycloalkyl, CONR, NR; W = H, CF3, CN, alkyl alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, halogen, amino, alkyloxy, aryloxy, acyl, carboxy, carboxamido, etc.] were prepared for use as 5 $\alpha$ -reductase inhibitors (no data). Thus, benzo[c]quinolizin-3-one II was prepared in a two step sequence which comprised N-alkylation of 6-chloro-3,4-dihydro-2(1H)-quinolinethione with Et vinyl ketone using K<sub>2</sub>CO<sub>3</sub> and 18-crown-6 in THF and intramol. cyclocondensation of the resulting N-(3-oxopentyl)quinolinethione using Me<sub>2</sub>SO<sub>4</sub> and DBU in toluene.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:50074 CAPLUS

DN 132:93206

TI Preparation of aminoalcohols and aminoketones as CNS active agents

IN **Guarna, Antonio**; Pupi, Alberto; Berti, Giovanna; Bottoncetti, Anna; Menchi, Gloria

PA Universita degli Studi di Firenze, Italy

09593173

SO Eur. Pat. Appl., 25 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 972764	A1	20000119	EP 1999-113902	19990716
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	IT 1304874	B1	20010405	IT 1998-FI171	19980717
PRAI	IT 1998-FI171	A	19980717		
OS	MARPAT 132:93206				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; R1, R2 = H, alkyl, alkenyl, etc.; R1 and R2 can be linked together to form an imide or amide cyclic system (Cy) selected from II, III, IV, etc.; A = O, OR, NR3R4 (wherein R, R3, R4 = H, alkyl, alkenyl, etc.); Q = a single bond, alkyl, alkenyl, etc.; W = H, alkyl, alkenyl, etc.; n = 1-4; m = 0-1; provided that at least one of the substituent W is always an halogen atom; when A = OR and R = aryl, R1 and R2 cannot be H and C1-4 alkyl; when m = 1, Q = single bond and n = 1 or 2, W cannot be Ph] which interact with CNS receptors and can be used as drugs for the treatment of CNS diseases or, if opportunely labeled, with radioactive isotopes, as radioligands or tracers to study CNS receptors in vitro and in vivo, were prepared Thus, reacting benzaldehyde with 3-(2-bromo-4-fluorophenyl)-3-hydroxypropylamine in the presence of NaBH3CN afforded V which showed an affinity for both S2 and D2 receptors with IC50 of 18.7  $\mu$ M in the S2 assay and IC50 of 34  $\mu$ M in the D2 assay.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT



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=> s e3

L14 1 WO9933828/PN

=> d bib abs hitstr

L14 .ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:542448 CAPLUS

DN 127:220585

TI Benzo[c]quinolizine derivatives, their preparation and use as  
5 $\alpha$ -reductases inhibitors

IN Guarna, Antonio; Serio, Mario

PA Applied Research Systems ARS Holding N.V., Neth. Antilles; Guarna,  
Antonio; Serio, Mario

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DT Patent

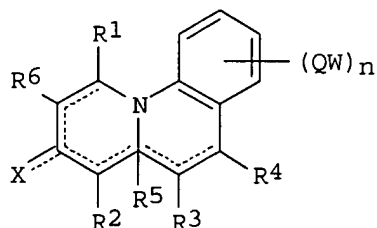
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9729107	A1	19970814	WO 1997-EP552	19970207
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2245758	AA	19970814	CA 1997-2245758	19970207
	AU 9717672	A1	19970828	AU 1997-17672	19970207
	AU 711886	B2	19991021		
	EP 880520	A1	19981202	EP 1997-903230	19970207
	EP 880520	B1	20030416		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EE 9800233	A	19981215	EE 1998-233	19970207
	EE 4058	B1	20030616		
	CN 1210536	A	19990310	CN 1997-192097	19970207
	CN 1116296	B	20030730		
	JP 2000504680	T2	20000418	JP 1997-528158	19970207
	SK 283299	B6	20030502	SK 1998-1044	19970207
	AT 237614	E	20030515	AT 1997-903230	19970207
	PT 880520	T	20030731	PT 1997-903230	19970207
	ES 2192263	T3	20031001	ES 1997-903230	19970207
	PL 187618	B1	20040831	PL 1997-328123	19970207
	EP 926148	A1	19990630	EP 1997-122733	19971223
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	NO 9803444	A	19980724	NO 1998-3444	19980724
	US 6303622	B1	20011016	US 1998-117583	19980729
	CA 2315055	AA	19990708	CA 1998-2315055	19981221
	WO 9933828	A1	19990708	WO 1998-EP8582	19981221
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				

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	CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
AU 9924194	A1 19990719	AU 1999-24194 19981221
AU 744105	B2 20020214	
BR 9813836	A 20001010	BR 1998-13836 19981221
EP 1066284	A1 20010110	EP 1998-966711 19981221
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AB The benzo[c]quinolizine derivs. I (R1-R4, R6 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycle, halo, amino azide, alkoxycarbonyl, etc.; R5 = H, alkyl, alkoxycarbonyl, cyano, aryl, heterocycle; X = O, acyl, alkoxycarbonyl, NO2, carbamoyl; Q = bond, alkyl, alkenyl, alkynyl, amino, etc., W = H, alkyl, alkenyl, alkynyl, aryl, aryloxy, amino, halo, etc.) were prepared as 5 $\alpha$ -reductases inhibitors (no data). Thus, N-(tert-butoxycarbonyl)-2-ethoxy-1,2,3,4-tetrahydroquinoline was cyclized with 2-(trimethylsilyloxy)-1,3-butadiene to give 1,2,4,4a,5,6-hexahydro-(11H)-benzo[c]quinolizin-3-one.